Remarks

Amendments to the Claims

Through an inadvertent clerical error, the claims amended in the response filed July 5, 2006 were not claims 10, 11, and 12 of this case but those of Serial No. 10/618,084, which are similar in format. The amendments intended to be made to claims 10, 11, and 12 of the present application are therefore re-presented in this response.

Claims 10 and 11 are amended to recite a method of "reducing" rather than "preventing" neuronal cell death. Paragraph [44] on page 54 of the specification supports this amendment: "Nucleic acids and the corresponding encoded proteins of the markers of the present invention can be used therapeutically in a variety of modes. . . . Such administrations can be used to reduce or eliminate cell death . . . ." Dependent claim 12 is amended to delete "subject" and recite "mammal," which has antecedent basis in claims 10 and 11.

Applicants also have canceled claims directed to non-elected subject matter and have deleted the non-elected subject matter from claims 10 and 11.

Please enter the amendments. They require no new search and do not introduce new matter.

Rejection of Claims 10-12 and 18 Under 35 U.S.C. § 112 ¶ 1

The Final Office Action maintains the rejection of claims 10-12 and 18 under 35 U.S.C. § 112 ¶ 1 as not enabled. Claim 18 has been canceled. Applicants respectfully traverse the rejection of claims 10-12.

The enablement requirement of 35 U.S.C. § 112, first paragraph states that a patent specification must teach a person skilled in the relevant art how to make and use the invention

claimed. The proper standard for determining whether the present specification meets the enablement requirement is whether any experimentation which may be needed to practice the methods of claims 10-12 is undue or unreasonable. *In re Wands*, 858 F.2d 731, 736-37, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to methods of reducing neuronal cell death in a mammal. Independent claim 10 recites administering to the mammal a nucleic acid molecule comprising a coding sequence for the neuronal marker (NM) acetylcholine receptor alpha 5. Independent claim 11 recites administering to the mammal purified acetylcholine receptor alpha 5 protein. The U.S. Patent and Trademark Office has the initial burden to establish a reasonable basis to question the specification's enablement of the claims. *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). To make a *prima facie* case of non-enablement using this standard, an Examiner must properly construe the claims and must weigh all the evidence and establish a reasonable basis to question the enablement provided in the specification for the claimed invention. M.P.E.P. §§ 2164.04 and 2164.05, 8th ed., revised August, 2006.

The Examiner has applied the wrong standard to the enablement analysis of this application. The Examiner continues to require the type of disclosure which would be required by the FDA to approve clinical use of the invention. For example, the Final Office Action states, without citing any case law, "It is noted that for a therapy claim to be enabled, there has to be evidence of therapeutic effect . . . the evidence of therapy is required to support enabling disclosure." Final Office Action at page 22 ¶ 3. To the contrary, there is no requirement that an invention be actually reduced to practice, nor are working examples required to enable an invention. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987); *In re Long*, 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966).

The specification is directed to those skilled in the art. With the response filed July 5, 2006 Applicants provided forty-four references which attest to the ability of those skilled in the art in July 2003, when this application was filed, to transfer and express exogenous genes effectively in neurons *in vivo*. Applicants also provided sixteen references which attest to the ability of those skilled in the art to administer proteins effectively to reduce or prevent neuronal death *in vivo* at the time the application was filed. Because it is closer to the filing date of the application, this evidence is far more relevant than the 1995-1999 references on which the Final Office Action relies. The Final Office Action points to only two references (Shah[1] and Thomas[2]) as being "close to the filing date." Final Office Action at page 22 ¶ 1. Neither reference is probative. Shah describes clinical trials – again, requiring a higher standard than enablement – involving non-viral gene therapy for therapeutic angiogenesis in humans with myocardial ischemia and peripheral vascular disease; these trials are not relevant to the claimed methods of reducing neuronal death. Thomas, although published closer to Applicants' July 2003 filing date, in May 2003, reviews earlier gene therapy research and is therefore no more relevant than the earlier published primary references cited by the PTO.

[1] Shah *et al.*, *Adv. Genetics 54*, 339-61, 2005.

[2] Thomas *et al.*, *Nature 4*, 346-58, 2003.

All the evidence of record must be considered in its entirety. *In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). When correctly analyzed, the weight of evidence of record in this application favors a finding of enablement of claims 10-12. Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

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